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EXAMINER	
SASAN, ARADHANA	
ART UNIT	**PAPER NUMBER**
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,233	BERTELSEN ET AL.	
	Examiner	Art Unit	
	Aradhana Sasan	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67-83,85-96 and 108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67-83, 85-96, and 108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 07/17/2007 are acknowledged.

2. In the remarks filed on 07/17/2007, claims 67, 69 were withdrawn. However, only claims 97-107 can be considered withdrawn (from the response to restriction requirement filed 03/12/2007).

3. Claim 84 was cancelled.

4. Claims 67-83, 85-96 and new claim 108 are included in the prosecution.

Response to Arguments

Rejection of claims 78, 81, 82, 84, and 89 under 35 USC § 112, second paragraph

5. Applicant's amendments of claims 78, 81, 82, 84, and 89 to remove the objectionable terms have rectified the indefiniteness under 35 USC § 112, second paragraph. The rejection of 04/19/2007 is withdrawn.

Rejection of claims 67-96 under nonstatutory obviousness-type double patenting

6. Applicant's arguments with respect to the rejection of claims 67-96 under nonstatutory obviousness-type double patenting have been fully considered but are not found persuasive. The rejection of 04/19/2007 is maintained.

Rejection of claims 67-72, 74-78, and 81-95 under 35 USC § 103(a)

7. Applicant's arguments with respect to the rejection of claims 67-72, 74-78, and 81-95 under 35 USC § 103(a) as being unpatentable over Penkler et al. (US 5,854,226 - the '226 patent) have been fully considered. Applicant notes the differences between the present claims and the sieving described in the '226 patent. Applicant states that the

'226 patent only teaches screening of the components NSAID and cyclodextrin, not of the whole composition and that the present claims do not require screening of the composition, nor of the active ingredients. However, one with ordinary skill in the art would use different particle sizes of the powder and screening the components is one method of controlling the particle size of components. Similarly, one skilled in the art would screen the final composition in order to control the particle size for the desired application. Therefore, even though the '226 patent discloses screening of the components, it would be obvious to one skilled in the art that screening would control the particle size of the composition.

Applicant argues that the conditions for contacting the powder with an aqueous medium are important and not taught or suggested by the prior art. Applicant argues that the cited art would not lead in the direction of the claimed invention. However, the '226 patent teaches the gradual addition of deionised purified water to the active ingredient (NSAID) mixture which meets the limitation of contacting the powder with an aqueous medium.

Since the limitations of instant claims are obvious over the teaching of the '226 patent, applicant's arguments are not found persuasive. The rejection of 04/19/2007 is maintained.

Rejection of claims 79-80, and 96 under 35 USC § 103(a)

8. Applicant's arguments with respect to the rejection of claims 79-80, and 96 under 35 USC § 103(a) as being unpatentable over Penkler et al. (US 5,854,226 - the '226 patent), and further in view of Skinhøj et al. (US 6,599,529 – the '529 patent) have been

fully considered. Applicant states that the '529 patent and the present application have a common inventor, are owned by the same entity or subject to an obligation of assignment to that entity. The '529 patent is disqualified under § 103(c) as "prior art" under § 103(a). The rejection of 04/19/2007 is withdrawn.

Rejection of claim 73 under 35 USC § 103(a)

9. Applicant's arguments with respect to the rejection of claim 73 under 35 USC § 103(a) as being unpatentable over Penkler et al. (US 5,854,226 - the '226 patent), and further in view of Penkler et al. (WO 95/32737 – the '737 publication) have been fully considered. Applicant argues that it would not be obvious to combine the teachings of the '226 patent and the '737 publication and arrive at the present invention because the methods for making the products of the '226 patent and the '737 publication are different and only post-factual hindsight would lead one skilled in the art to combine the technical methodology of the two references. The '226 patent teaches the limitations of particle size and the gradual addition of water to the active ingredient powder. The deficiency in the '226 patent is that it does not specifically include an organic solvent as part of the aqueous medium. The '737 publication teaches a paste composition comprising an NSAID and a cyclodextrin that is made with a wetting solution which may include an organic solvent such as a lower alkanol. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the

claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Therefore, the rejection of 04/19/2007 is maintained.

MAINTAINED REJECTIONS:

The following is a list of maintained rejections:

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 67-83, 85-96, and new claim 108 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 8-17, 22-29, and 34-37 of U.S. Patent No. 6,713,089 ('089 hereafter). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claim limitations of each of the instant claims 67-96 would be obvious over '089.

Instant claims 67-70, and 75 would be obvious to a person with ordinary skill in the art over claim 1 of '089 which covers the claim limitations of: solubility of the active (at the most 0.1% w/v in 0.1N hydrochloric acid at room temperature), particle size of the active (at least 90% w/w of the active particles pass through a 180 μm sieve), pK_a of the active (at the most 5.5), particulate composition formed after powder contacting an aqueous medium, particle size of the particulate composition (at least 50% of the particles pass through a 180 μm sieve), release rate of the active (at least 50% w/w within the first 20 minutes) using the 0.07 N hydrochloric acid as the dissolution medium, and the composition comprising a pharmaceutically acceptable excipient. The difference between the instant claims and those of '089 is that '089 claim 1 discloses that when the dissolution of the pharmaceutical composition is tested, the active substance "dissolves", as opposed to "releases" as in instant claim 67. A person having ordinary skill in the art would find that when a pharmaceutical composition is subjected to a particular dissolution test, and a certain percentage of the active ingredient "dissolves", it means that the active ingredient is "released" from the pharmaceutical composition into the dissolution medium.

Instant claim 71 (with the release rate limitation of at least 55% w/w of active within the first 20 minutes of the dissolution test) would be obvious to a person with ordinary skill in the art over claim 2 of '089. The difference between "dissolves" and "releases" is discussed above.

Instant claims 72, 73, and 74 (with the limitations of solubility of the active as at the most 0.05% w/v in 0.1N hydrochloric acid at room temperature, aqueous medium components water and organic solvent, and particle size of the particulate composition as 250 μm) would be obvious to a person with ordinary skill in the art over claims 3, 8, and 9 of '089.

The limitations of instant claims 76-96 (excipients, filler having binding properties, calcium hydrogen phosphate as filler, mean particle size of filler at the most 140 μm, alkaline substances, antacid-like substances, sodium hydrogen carbonate, mean particle size of antacid-like substance at the most 250 μm, NSAID (non-steroid anti-inflammatory drug) as an active substance, lornoxicam as an NSAID, further active drug substances (paracetamol etc.), dosage of active in the composition (1mg – 1.6g), dosage of lornoxicam in the composition (4, 3, 12, 16, 20, 24, 28, 32 or 36mg), water content of the composition at the most 5% w/w, and calcium hydrogen phosphate) would be obvious to a person with ordinary skill in the art over claims 10-17, 22-29, and 34-37 of '089.

Since the instant application claims a quick release pharmaceutical composition and the claim limitations of the composition (active, alkaline substance, particle size, release rate, particulate composition, excipients), it is obvious over claims 1-3, 8-17, 22-29, and 34-37 of '089 and thus, they are not patentably distinct over each other.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 67-72, 74-78, and 81-83, and 85-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penkler et al. (US 5,854,226, '226 hereafter).

The claimed invention is a quick release (at least 50% w/w of the active within the first 20 minutes of a dissolution test) pharmaceutical composition for oral administration, comprising an active substance, such as the non-steroidal anti-inflammatory drug (NSAID) lornoxicam, that is poorly soluble (solubility of at the most 0.1% w/v in 0.1 N hydrochloric acid at room temperature), and is a weak acid (pK_a at the most 5.5). The composition is based on a powder (with a particle size where at least 90% of the particles of the powder pass through a 180 μm sieve), which contacts an aqueous medium to form a particulate composition (with a particle size where at least 50% w/w of the particles pass through a 180 μm sieve).

Penkler et al. (US 5,854,226, '226 hereafter) teaches a pharmaceutical composition for oral administration comprising an inclusion complex of a non-steroidal anti-inflammatory drug (including lornoxicam), an alkaline earth metal bicarbonate, and further active ingredients.

The particle size claim limitation in instant claims 67-70, and 74 is obvious over '226. '226 teaches "pre-screened NSAID" (Col. 3, lines 65-66), and in example 4,

teaches that the lornoxicam is screened (30 mesh) (Col. 5, lines 66-67). The 30-mesh screen is equivalent to a 600 μm sieve (according to the U. S. standard mesh sieve sizes provided by the ASTM), while instant claim 1 uses a 180 μm sieve (or an 80-mesh screen). A person having ordinary skill in the art at the time the invention was made would have found it obvious to use different particle sizes of the powder and the particulate composition in order to optimize the release profile. In order to enhance the quick release, a finer particle size (or a finer mesh screen) would be used to allow faster release of the active from the composition.

The instant specification discloses that the solubility of lornoxicam "is < 1 mg/100ml in 0.1 N HCl" (Page 6, lines 1-3) and "the pK_a value of lornoxicam is about 4.7" (Page 14, line 27). Since '226 uses lornoxicam as the active substance in the pharmaceutical composition (Col. 2, lines 31-34), a person having ordinary skill in the art would find the lornoxicam active in the instant application as an obvious component of the composition. Therefore, the solubility limitation of the active substance in instant claims 67-68, and 72, and the pK_a limitation of the active substance in instant claims 69-70 would be obvious over '226 because the same active is used in the reference application.

'226 teaches the "gradual addition of deionised purified water" to the pre-screened NSAID mixture (Col. 4, lines 1-2). Therefore, the claim limitation of the powder being contacted with an aqueous medium of instant claims 67-70 is obvious over '226. Water as an aqueous medium would be obvious to one skilled in the art. The claim limitation of the particle size of the particulate composition (after the powder has been

contacted with an aqueous medium), would have been obvious to one skilled in the art because the particle size of the powder prior to contact with an aqueous medium would be increased as a result of the "wetting process".

Regarding instant claims 67-70, the release rate limitation of would have been obvious to one skilled in the art over '226. '226 teaches a dissolution rate of lornoxicam as 80% dissolved within 30 minutes, using purified water (pH ~6.5, temperature 37°C) (Col. 6, lines 24-28, Fig. 2, Example 5). Instant claims 67-70 recite a "release" rate of 50% w/w of the active substance within the first 20 minutes at an acidic pH (0.07N hydrochloric acid) dissolution medium. A person skilled in the art would have found it obvious to test the dissolution/release of the active at various pH levels (especially acidic pH levels which are present in gastric conditions) during the process of routine optimization to ensure that the active will be absorbed by the circulatory system.

Regarding instant claim 71, the claim limitation of the 55% w/w release rate within the first 20 minutes would have been obvious to one skilled in the art given the '226 teaching of dissolution rate. Also, during the process of routine optimization, a person skilled in the art would modify the formulation parameters in order to optimize the dissolution/release rate. See MPEP 2144.05.

Regarding instant claims 75-78, a person skilled in the art would find the excipient and filler having binding properties limitations obvious over '226 which teaches that the "pharmaceutical composition may also contain conventional excipients including binders ... diluents such as lactose, disintegrating agents, ... lubricants" (Col. 2, lines 50-54).

Regarding instant claims 81-83, and 95, a person skilled in the art would find the alkaline substance, sodium hydrogen carbonate (elected species), obvious over '226 which teaches "the alkali agent is preferably sodium hydrogen carbonate" (Col. 2, line 45). The mean particle size limitation of instant claim 83 would be an obvious variant to one skilled in the art during the process of routine optimization.

Regarding instant claims 85-87, a person skilled in the art would find the NSAID lornoxicam obvious over '226 which teaches lornoxicam in the pharmaceutical composition (Col. 2, lines 31-34, Col. 5, line 66, Example 4, Col. 6, lines 10-28, Example 5, and line 42, claim 1).

Regarding instant claims 88-90, a person skilled in the art would find the further active drug substance obvious over '226 which teaches a further active drug substance, including paracetamol (Col. 8, lines 9-12)

Regarding instant claims 91-93, a person skilled in the art would find the dosage of the active substance obvious over '226 which teaches unit compositions of lornoxicam (Figure 2 with 4mg of lornoxicam). One skilled in the art would vary the dosage of the active ingredient, lornoxicam, in order to optimize the release/dissolution profile, and stability. The dosages recited in instant claims 91-93 would have been obvious variants absent any criticality or unexpected results.

Regarding instant claim 94, a person skilled in the art would find the water content limitation of at the most 5% w/w obvious over '226 which teaches a drying step after the addition of water and mixing (Col. 4, line 9). A person skilled in the art would reduce the water content of the composition in order to improve shelf life and minimize

interactions and leaching, therefore, the water content limitation would have been an obvious variant found during routine optimization.

14. Claim 73 is rejected under 35 U.S.C. 103(a) as being unpatentable over Penkler et al. (US 5,854,226), and further in view of Penkler (WO 95/32737, '737 hereafter).

The teaching of '226 is stated above.

'226 does not specifically include an organic solvent as part of the aqueous medium.

A person skilled in the art would have found the limitation of the aqueous medium comprising water and an organic solvent obvious over '226, in view of '737. '737 teaches a pharmaceutical composition comprising a NSAID and a cyclodextrin and forming a paste with these ingredients and a "wetting solution". This wetting solution "may be selected from water, a lower alkanol, ... or a mixture of water and a lower alkanol" (Page 7). A person skilled in the art would be motivated to include a lower alkanol as an organic solvent along with water during the process of routine experimentation to make a particulate composition given the '737 teaching that a lower alkanol may be used in a wetting solution (or aqueous medium).

NEW REJECTIONS:

The following is a list of new rejections:

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 79-80, and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penkler et al. (US 5,854,226) in view of Sallman et al. (US 4,296,128).

The teaching of Penkler is stated above.

Penkler does not expressly teach calcium hydrogen phosphate.

Sallman teaches calcium hydrogen phosphate in tablet compositions (Col. 11, line 28).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the composition with lornoxicam and the powder contacting the aqueous medium, as suggested by Penkler, combining it with calcium hydrogen phosphate in tablet compositions, as suggested by Sallman, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because calcium hydrogen phosphate is a suitable carrier for tablet formulations (Col. 11, lines 24-28).

Conclusion

17. Due to the new grounds of rejection, this action is made non-final.

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-

9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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